Beginning this year, Jane Buckner, MD, became president of Benaroya Research Institute at Virginia Mason (BRI). Dr. Buckner, an internationally known researcher in autoimmune diseases, succeeds Gerald Nepom, MD, PhD, who served as director for 30 years and stepped down from the position.

Dr. Buckner joined BRI in 1999 and has served as associate director since 2012. She brings an interdisciplinary approach — genetics, immunology and clinical medicine — to understanding the causes and potential cures of autoimmune diseases. Her areas of specialty include type 1 diabetes, multiple sclerosis, rheumatoid arthritis, lupus and relapsing polychondritis. Dr. Buckner also is a rheumatologist at Virginia Mason, the director for the BRI Translational Research Program, a principal investigator at BRI and an affiliate professor at the University of Washington.

What are your scientific goals for BRI?

BRI has built its reputation and renown in a unique niche in medical research through our integrated focus on autoimmune diseases, which extends to other diseases of the immune system. Our teams of scientists create a synergy, allowing us to ask much more complex questions than we could ask in isolation. This has resulted in breakthroughs in basic and translational immunology that we then apply to multiple diseases of the immune system. In the future we plan to expand our studies to more autoimmune diseases, to develop new tools to study these diseases and recruit scientists with expertise that will complement this work and allow us to achieve more, faster. Our aim is to eliminate these lifelong, chronic diseases, not just treat the symptoms.

What excites you about the future of autoimmune diseases research?

When I started at BRI years ago, I never imagined we could make the research advances that we’ve made. Today, we’re conducting clinical trials to see if we can stop type 1 diabetes before it starts. We’re investigating if we can alter the genes in a patient’s cell to stop them from causing disease. We’re figuring out how to take a drop of an individual’s blood and determine his or her risk for immune system diseases. If the person is at risk, we hope to prevent or halt the onset of disease, determine the most effective medication, track how it’s working, and modify it if needed to ensure the best outcome possible. This is a very exciting time in immunology research.

Why is it important to you to continue seeing patients at Virginia Mason?

There are three reasons it’s important for me to continue my medical practice. First, I really enjoy seeing patients. The very personal interaction is important to me. Second, it’s really wonderful to experience science in action by...
For most people, the onset of type 1 diabetes (T1D) seems to occur suddenly, often resulting in a trip to the emergency room with life-threatening complications. TrialNet, a worldwide leader in type 1 diabetes research, is working to change that scenario with a new type 1 diabetes staging classification system.

The new staging classification is vital to understanding how type 1 progresses, says Carla Greenbaum, MD, director of BRI's Diabetes Research Program and chair of TrialNet. Equally important is TrialNet's ability to diagnose the disease in its earliest stages, allowing for prompt intervention.

“Identification of the pre-symptom stages of type 1 diabetes can be compared to identification of high blood pressure as a predictor of heart attack and stroke,” notes Dr. Greenbaum. “Before treatment for high blood pressure became commonplace, we were missing a key tool to prevent heart disease. Today, people can receive intervention long before they experience symptoms or significant complications. The same is now true for type 1 diabetes.”

In the Jan. 2016 issue of Diabetes Care, the JDRF, American Diabetes Association (ADA) and Endocrine Society recommended adoption of a new type 1 diabetes staging classification. This recommendation is largely based on two decades of TrialNet research involving more than 150,000 relatives of people with type 1 diabetes. TrialNet, funded by the National Institutes of Health, is an international network of leading academic institutions, physicians, scientists and healthcare teams at the forefront of type 1 diabetes research. BRI has been involved with TrialNet since the network's inception in 2001 and directs the TrialNet Clinical Network Hub and the TrialNet Northwest Clinical Center.

“TrialNet’s goal is to identify the disease at its earliest stage, delay progression and ultimately prevent it. We offer screening and clinical trials for every stage of type 1 diabetes and also close monitoring for disease progression,” explains Dr. Greenbaum.

Type 1 diabetes can now be most accurately understood as a disease that progresses in three distinct stages.

**Stage 1** is the start of type 1 diabetes — there are no symptoms and blood sugar remains normal. Individuals test positive for two or more diabetes-related autoantibodies. The immune system has already begun attacking the insulin-producing beta cells.

In **Stage 2**, like stage 1, there are no symptoms and individuals have two or more diabetes-related autoantibodies. But now, blood sugar levels have become abnormal due to increasing loss of beta cells. For both stages 1 and 2, there is nearly a 100 percent risk of developing type 1 diabetes.

**Stage 3** is when individuals generally show common symptoms of type 1 diabetes, which include frequent urination, excessive thirst, weight loss and fatigue. Clinical diagnosis has typically taken place by this time and there is significant beta-cell loss.

Clinical research supports the usefulness of diagnosing type 1 diabetes early. The sooner diagnosis is made in the disease process, the earlier intervention can take place, and the more beta cells are likely to remain. More beta cells may lead to better outcomes regarding blood sugar control and reduction of long-term complications.

For people who participate in type 1 diabetes prevention research like TrialNet, the risk of diabetic ketoacidosis (a life-threatening diabetes complication) at diagnosis decreases from 30 percent to less than 4 percent. Family members of people with type 1 diabetes have a 15 times greater risk of being diagnosed than a person with no family history. Learn more about screening at TrialNet.org and BRI's diabetes research program at BenaroyaResearch.org.

**NEW HOPE FOR T1D EARLY INTERVENTION**
Benaroya Research Institute (BRI) and Seattle Children’s Research Institute (SCRI) are pioneering the use of gene editing techniques in efforts to control type 1 diabetes (T1D). “This research could be an enormous asset in developing future therapies for many autoimmune diseases like type 1 diabetes, multiple sclerosis, rheumatoid arthritis and more,” says BRI President Jane Buckner, MD.

Dr. Buckner, BRI’s Gerald Nepom, MD, PhD, SCRI’s Director of the Center for Immunity and Immunotherapies David Rawlings, MD, and SCRI’s Andrew Scharenberg, MD, are the lead investigators of the $1 million grant from The Leona M. and Harry B. Helmsley Charitable Trust.

**Gene Editing**

“This is a preclinical study in the laboratory where we take cells that recognize the pancreas from people with type 1 diabetes,” explains Dr. Buckner. “We engineer or edit the genes in the cells so they become regulatory T cells. Importantly, they will remain regulatory T cells in the body so we can use them therapeutically. The long-term goal would be to take cells from a person who has type 1 diabetes or is at high risk for the disease. We would remove cells from their blood, edit the cells that would attack the islet cells in the pancreas and turn them into regulatory T cells. Then we would inject them back into the patient’s bloodstream, and they would travel to the pancreas and stop any T cell attacks in the pancreas.

“This research could lead to fundamentally new ways to prevent loss of immune system regulation, a common problem in autoimmune diseases like type 1 diabetes where the body’s own immune system attacks and destroys the islet cells in the pancreas that make insulin,” says Dr. Buckner. People with type 1 diabetes must inject themselves with insulin in order to stay alive.

**Strong Collaboration**

BRI and Seattle Children’s have collaborated on numerous projects. In this study, BRI brings its regulatory T cell expertise to combine with SCRI’s gene editing expertise to attack this complex problem. Previously in laboratory testing, BRI scientists discovered a means to create regulatory T cells that have the potential to control unwanted immune responses such as those that lead to autoimmune diseases. The scientific team used tetramer technology, developed by BRI, to identify and purify small populations of white blood cells that can be converted to T regulatory cells. Scientists recently found that these regulatory T cells lose their effectiveness over time and are now looking for a way to maintain the cells as regulatory T cells through gene editing.

**T Cell Therapy**

Regulatory T cells are white blood cells that can block the activation of other harmful T cells and thus regulate the immune system, avoiding autoimmune diseases. The benefit of using regulatory T cells for therapy is that it can focus immune suppression on a specific area without impairing the entire immune system, a key objective for treating and curing autoimmune diseases. Currently, most immune therapies are not very targeted and suppress the body’s entire immune system, leaving the body vulnerable to infections, bacteria and viruses. For more information, visit BenaroyaResearch.org.
t’s always been about the smile for Chris Boerner. At age 14, as a freshman in high school, she stopped being able to smile. It took ten years for her to recover her smile.

Chris was diagnosed with myasthenia gravis (MG), an autoimmune disease that occurs when the immune system attacks the body’s connection between nerve and muscle. MG causes weakness in the muscles that control the eyes, face, neck and limbs. People may have difficulty with partial paralysis of eye movements, double vision and droopy eyelids, as well as weakness and fatigue in the neck and jaws. They may experience problems in chewing, talking, swallowing, breathing and holding up their head. MG may also affect people’s arms and legs.

“When I was diagnosed I couldn’t lift my head off the pillow. My neck muscles were too weak,” says Chris. “I had trouble talking, eating, swallowing and smiling. When I tried to smile it looked like I was crying. I was taking prednisone for the disease, and it caused me to have a triple chin. This is not a great way to be when you’re in high school.”

Chris had surgery to remove her thymus gland, and they told her it may take time before she can smile. Ten years after her surgery she could smile again, and her medications eventually kept her disease under control.

She now has a lot to smile about. She’s married and has two young children. She was a leader at Starbucks in strategy and marketing, but about three years ago she decided she wanted to produce a product to connect with people. She remembered how her dad gave her a pill holder that she treasured for many years. It made her feel confident. Chris developed a pill holder in several fashionable styles and launched her company, Cielo Pill Holders, CieloPillHolders.com. She will soon be featured in an Amazon exclusives video.

Chris learned about Benaroya Research Institute’s fight against autoimmune diseases at a fundraising event and determined she would give 5 percent of her proceeds to BRI. “I’m very hopeful that BRI can help people through earlier diagnosis and better treatments, and eventually eliminate autoimmune diseases.

“It’s been an incredible experience for me to produce these pill holders,” says Chris. “I have heard from many people who have to take medication several times a day that the pill holders have helped them. They’re beautifully designed, easy to open and can be a necklace or hang on your key chain. I’m so glad I can give back and support research for the many people who suffer from lifelong chronic diseases. I’ve been so fortunate and now I’d like to help others.”

For more information on giving to BRI, visit BenaroyaResearch.org.

Chris Boerner wears one of her Cielo pill holders. She is donating 5 percent of her business’s proceeds to BRI for autoimmune diseases research.
NEW PRESIDENT
Continued from front page

Treating patients and seeing them get better. Because I’m a rheumatologist and treat chronic diseases, I’ve cared for some of my patients for 20 years. This gives me insight into the natural history of the disease, the path these patients follow and issues that go beyond making the initial diagnosis and therapy. This informs my work as a scientist. Third, I partner with Virginia Mason physicians to learn about their patients, understand their perspective and build relationships for our research at BRI.

What are you most proud about as a leader of BRI?

I get compliments all the time from the outside scientific community about how unique we are and that we do research the right way. For the size of our institution, we’re well recognized and play a leadership role in important consortiums such as the Immune Tolerance Network and Type 1 Diabetes TrialNet. I’m proud other scientists reach out to collaborate with us from the University of Washington, Stanford, Yale and even universities in Europe and Japan. I’m proud that we’re a leader in improving the lives of people with autoimmune and immune system diseases — from predicting and preventing onset of disease to more effective customized medical treatments to getting close one day to eliminating these devastating diseases. And I’m inspired by the support we receive from our community.

How has the community supported BRI?

Financial donations are central to our ability to do cutting-edge research. Without that support we wouldn’t be able to innovate for breakthrough discoveries and to do projects that are higher risk and higher reward. Many members of the community also participate in our clinical trials and biorepositories. We really appreciate people taking the time and effort to get involved in research. We also have board members and other committee volunteers — an amazing group of people — who are willing to donate their energy and expertise to help us succeed in our mission. It’s inspiring to know the community supports us and is committed to our research.

STEVE ZIEGLER LEADS ACADEMIC AFFAIRS

In addition to his role as BRI’s Director of the Immunology Research Program for the past 13 years, Steve Ziegler, PhD, assumed the new position of director of Academic Affairs at BRI, as of Jan. 1. In this role, he will oversee faculty recruitment and development and serve as chair of the faculty appointment and promotion committee. Dr. Ziegler will also develop and expand external academic relationships, including BRI’s local affiliations with the University of Washington, Fred Hutch and Center for Infectious Disease Research as well as institutions around the country such as La Jolla Institute for Allergy and Immunology.

What is the importance of BRI’s academic ties?

We have numerous collaborations with local scientific institutes including Seattle Children’s Research Institute, Fred Hutch and the University of Washington as well as nationally and internationally, such as University of California, San Francisco, Stanford, Northwestern, Kings College London and University of Salzburg. These allow us to bring diverse expertise from many different people to work on complex problems. BRI has core laboratories, biorepositories with human samples, and experience with very large data sets that gives us the ability to work successfully with our collaborators and achieve more in unison.

What’s it like to be a scientist at BRI?

The people who work at BRI like to collaborate and are willing to take risks. They need to be confident, innovative and creative. Our goal is to support and retain our high quality researchers in doing the highest quality science to understand and improve human health. We all work together to support and build our scientific infrastructure so we have the tools we need to be successful. We educate and learn from one another and we are proud to speak at and lead scientific conferences all over the world.

How does BRI help educate scientists?

It’s an important part of our mission to educate and mentor the next generation of scientists and to encourage young people to enter this field. We provide undergraduate internships, mentor graduate students and engage postdoctoral trainees from all over the world. We enjoy the opportunity to train and mentor new people. We also learn and benefit from having their ideas, dedication and energy. One never knows where the next great idea is going to come from.

(Left to right) Hongwei Han, PhD, and Emma L. Kuan, PhD, postdoctoral trainees, with Steve Ziegler, PhD, and Jia Bin Tan, research technician.
LANDMARK STUDIES SHOW STRIDES AGAINST PEANUT ALLERGIES

The Immune Tolerance Network (ITN), led by Benaroya Research Institute (BRI), with Gerald Nepom, MD, PhD, as network director, has made major breakthroughs in fighting peanut allergies. A landmark study called LEAP (Learning Early About Peanut Allergy) demonstrated that regular peanut consumption begun in early infancy and continued until age five reduced the rate of peanut allergy in at-risk infants by 80 percent compared to non-peanut consumers. LEAP was the first large, well-controlled study to conclusively show the benefits of early peanut consumption in this at-risk population, changing previous notions about peanut allergy prevention.

Now, in a follow-up study called LEAP-ON, researchers found peanut allergy prevention achieved from early peanut consumption in at-risk infants persists after a one-year period of avoiding peanut. The results were published March 4 in The New England Journal of Medicine.

“"This study offers reassurance that eating peanut-containing foods as part of a normal diet — with occasional periods of time without peanut — will be a safe practice for most children following successful tolerance therapy," says Dr. Nepom.

ITN STUDIES CHOSEN FOR RECOGNITION

The LEAP study manuscript was selected by The New England Journal of Medicine as one of the most notable articles of 2015. ITN's LEAP and HALT-MS studies were chosen as two of 15 highlighted research advances for 2015 by the National Institute of Allergy and Infectious Diseases (NIAID). In HALT-MS, 25 individuals with relapsing-remitting multiple sclerosis (MS) received high-dose immunosuppression followed by an autologous stem cell transplant to potentially reset their immune systems in a noninflammatory manner. At three years, 80 percent of participants showed sustained remission despite not being on other MS therapies.

For more information, visit BenaroyaResearch.org.